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Symptom Experiences in Metastatic Breast Cancer Patients: Relationships to Activity Engagement, Value-based Living, and Psychological Inflexibility

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Abstract

Objective—This study examined symptom-based subgroups of metastatic breast cancer (MBC) patients and the extent to which they differed across key constructs of Acceptance and Commitment Therapy (ACT).

Methods—Eighty women with MBC completed self-report surveys assessing ten common symptoms and several ACT variables (i.e., activity engagement, psychological inflexibility, value obstruction, and value progress) during a single time point.

Results—A cluster analysis yielded three patient subgroups: low symptoms, low-moderate symptoms, and moderate-high symptoms. Relative to the subgroup with low symptoms, the other subgroups reported less activity engagement. In addition, compared to patients with low symptoms, the subgroup with moderate-high symptoms reported greater psychological

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inflexibility (i.e., avoidance of unwanted internal experiences) and greater difficulty living consistently with their values.

Conclusions—Women with MBC show heterogeneity in their symptom profiles, and those with higher symptom burden are more likely to disengage from valued activities and avoid unwanted experiences (e.g., thoughts, feelings, bodily sensations). Findings are largely consistent with the ACT model and provide strong justification for testing ACT to address symptom interference in MBC patients.

Keywords

metastatic breast cancer; oncology; symptoms; activity engagement; acceptance and commitment therapy; psychological flexibility

Background

Medical advances have led to increasingly prolonged illness for metastatic breast cancer (MBC) patients [1], with many experiencing symptoms which impair their quality of life and functional capacity [2–6]. Common symptoms in this population include depression, anxiety, sleep disturbance, pain, and fatigue [6–10]. Research indicates that 36% of MBC patients experience depression, anxiety, or both [7]. Worsening depression has predicted increased sleep problems in MBC patients [10], with over 60% reporting at least one type of sleep disturbance [9]. Sleep problems are frequently associated with pain and fatigue, with over half of MBC patients reporting clinically significant levels of these symptoms [3, 6, 11]. Other common symptoms among cancer patients (e.g., nausea, neuropathy, swelling of arms and legs, hot flashes, cognitive problems) have received less attention in the MBC literature [6, 12–14].

Preliminary evidence suggests that symptoms may disrupt the daily activities of MBC patients [3, 15]. One study found that greater symptom severity and interference were associated with greater daily activity impairment and reduced work productivity in this population [3]. Another study of MBC patients found that greater depressive symptoms predicted increases in global perceptions of activity disruption over a 3-month period [15].

To date, intervention trials to reduce symptoms and distress have been largely ineffective for MBC patients [16]. According to a recent Cochrane meta-analysis [16], non-pharmacologic interventions for MBC patients, most of which were cognitive-behavioral or emotion-focused group therapy, have only yielded short-term benefits with respect to pain and distress reduction. Cognitive-behavioral therapy is a problem-focused approach with a primary goal of symptom reduction. Novel intervention models seek to shift the emphasis from symptom reduction to decreasing symptom-related suffering and interference with valued activities [17]. Given that symptom-related suffering and interference are focal points of palliative care for advanced cancer patients [18], these novel intervention models might be particularly well-suited for MBC patients.

One psychological intervention that holds promise for reducing symptom-related suffering and functional interference in cancer patients is Acceptance and Commitment Therapy

(ACT) [19]. ACT promotes psychological flexibility so that internal experiences (e.g., thoughts, feelings, bodily sensations) do not impair patients' ability to live a meaningful life [20]. Psychological flexibility is defined as the ability to fully experience the present moment, including thoughts and feelings, while persisting in value-based action [17]. This flexibility has been associated with reduced anxiety and depressive symptoms and better well-being in patients with common cancers [21, 22]. Conversely, psychological inflexibility occurs when people avoid unwanted thoughts and emotions, which often has the paradoxical effect of increasing distress and decreasing value-based action [17]. From an ACT perspective, values are patient-defined life directions (e.g., showing love, promoting justice) that are intrinsically reinforcing and provide a sense of meaning and purpose [17].

ACT has been successfully applied to a range of clinical disorders, including anxiety, depression, and posttraumatic stress disorder [23]. In addition, ACT has shown promising effects on psychological distress, quality of life, and self-management among patients with medical conditions such as diabetes and chronic pain [24, 25]. A small number of pilot studies—most of which were not randomized trials--have examined the efficacy of ACT in cancer patients [26]. However, one randomized trial with late-stage ovarian cancer patients found large improvement in mood and quality of life among ACT participants compared to those assigned to cognitive-behavioral therapy [27].

Despite the promising evidence presented above, several remaining questions need to be answered before investing resources into developing an ACT intervention for MBC patients. Most importantly, research is needed to establish links between key ACT constructs (i.e., activity engagement, psychological inflexibility, value obstruction, and value progress) and symptom burden in MBC patients. The current study aims to take this critical next step. Drawing upon ACT theory [17] and prior research [21, 22], we expected that patient subgroups with higher symptom levels would report less activity engagement, greater psychological inflexibility and value obstruction, and less value progress than subgroups with lower symptom levels.

Methods

Participants and procedures

Following institutional review board approval, MBC patients were recruited from an academic cancer center in the Midwestern United States between May and August 2015. Eligible patients were women with stage IV breast cancer who were fluent in English. Eligibility was confirmed via medical record review and consultation with oncologists. Research assistants mailed letters inviting study participation and consent forms to patients and called them to screen for eligibility and complete the informed consent process. Patients were excluded from study participation if they made three or more errors on a validated 6-item cognitive screener that has been widely used with cancer patients [28]. Sample items include "What year is this?" and "What month is this?" At the time of enrollment, patients received a brochure that described available mental health services at the cancer center.

Of the 107 MBC patients who received mailed information about this study, 85 (79%) completed the screening assessment, 12 (11%) could not be reached via phone, and 10 (9%)

refused study participation. Primary reasons for refusal were time constraints and health concerns. Of those who completed screening, two were found to be ineligible, and 83 were eligible and consented to participate.

Eighty patients (96%) completed a standardized phone assessment consisting of the measures described below. Patients received a $40 gift card for their participation.

Measures

Physical and psychological symptoms—Ten common physical and psychological symptoms were assessed. Four-item NIH Patient Reported Outcomes Measurement Information System (PROMIS) measures [29, 30] were used to assess the severity of the following symptoms: anxiety, depressive symptoms, sleep disturbance, fatigue, and general cognitive concerns. In addition, a 3-item PROMIS measure of pain intensity was utilized [30]. For all items, respondents selected one of five response options that best described their symptom level during the past 7 days. These measures have undergone rigorous reliability and validity testing [29–31]. PROMIS measures were initially developed with cancer patients' input [32], and a growing body of research has documented the measures' reliability and validity for use with cancer patients, including those with advanced disease [33–35].

PROMIS measures of nausea, hot flashes, swelling of arms or legs, and neuropathy have yet to be developed. Thus, alternative measures of these symptoms were used, including 11 questions from the Memorial Symptom Assessment Scale (MSAS) [36] to assess nausea, swelling of arms and legs, and neuropathy during the past week. In addition, a 3-item validated assessment of hot flashes during the past two weeks was used [37]. Questions for each of these measures first assessed the presence of a symptom (yes or no), followed by Likert-type scales to assess symptom frequency, severity, and distress or bother. For swelling and hot flashes, only severity and distress or bother were assessed.

Engagement in roles and activities—A 6-item PROMIS measure [29, 30] was utilized to assess engagement in roles and activities. Sample items are "I have to limit the things I do for fun with others" and "I have trouble doing all of my usual work (including work at home)." Items were rated on a scale from 5 (*never*) to 1 (*always*). Items were reverse scored and summed, with higher scores indicating greater engagement in roles and activities. As stated above, PROMIS measures have undergone extensive validation [29–31].

Psychological inflexibility—The 7-item Acceptance and Action Questionnaire-II (AAQ-II) [38] was used to assess psychological inflexibility or difficulty pursuing effective behavior when having unwanted internal experiences. A sample item is "My painful experiences and memories make it difficult for me to live a life that I would value." Items were rated on a scale from 1 (*never true*) to 7 (*always true*). The AAQ-II demonstrated good test-retest reliability and discriminant validity [38].

Value-based living—The Valuing Questionnaire (VQ) [39] consists of two, 5-item subscales assessing progress in living consistent with one's values (VQ Progress) as well as obstructions to doing so during the past week (VQ Obstruction). Sample items are "I made

progress in the area of my life I care most about" and "Difficult thoughts, feelings or memories got in the way of what I really wanted to do." Items were rated on a scale from 0 (*not at all true*) to 6 (*completely true*). The measure showed evidence of good internal consistency reliability and concurrent validity with measures of psychological well-being and ACT constructs [39].

Demographic and medical information—Patients reported their demographic information. Age, date of diagnosis, and treatments were collected from medical records.

Statistical analysis

Data were analyzed with the Statistical Package for the Social Sciences (SPSS, Version 23.0; IBM Corp, Armonk, NY). Descriptive statistics were used to characterize demographic and medical characteristics, symptoms, and ACT variables in the present sample. Intercorrelations were computed among main study variables. Then a hierarchical agglomerative cluster analysis (Ward's method, squared Euclidian distance) was conducted to determine patient clusters based on the severity of the ten symptoms. This analysis was performed because co-occurring symptoms have a compounding, negative effect on cancer patients' functional status and quality of life [40]. Thus, patients with higher symptom burden were expected to show worse study outcomes compared to those with lower symptom burden. Differences between the clusters on demographic and medical factors were assessed using Chi-square tests and one-way ANOVAs followed by Tukey HSD tests. One-way ANOVAs and Tukey HSD tests also were performed to examine differences between patient clusters on the ten symptoms, activity engagement, psychological inflexibility, value obstruction, and value progress. Two-sided p-values of .05 were considered statistically significant.

Results

Preliminary analyses

Sample characteristics are found in Table 1. The sample was primarily Caucasian, married, and college-educated with a wide range of income. Patients were, on average, 56 years old and had been diagnosed with stage IV breast cancer four years previously. The majority of patients had received chemotherapy, radiation, hormonal therapy, and surgery.

Descriptive statistics, Cronbach's alphas, and intercorrelations for the main study variables are found in Table 2. All measures showed acceptable internal consistency reliability (α range = .75 to .95). As expected, nearly all symptoms showed significant, negative associations with activity engagement. The only exceptions were nausea, neuropathy, and hot flashes, which were not significantly related to this outcome. A similar pattern of findings was obtained with respect to value obstruction, with most symptoms showing significant, positive associations with this outcome. Nausea, swelling of arms or legs, and hot flashes were the only symptoms unrelated to value obstruction. Additionally, half of the symptoms (i.e., nausea, fatigue, sleep disturbance, anxiety, and depressive symptoms) showed significant, negative associations with value progress. Finally, psychological inflexibility showed significant, positive associations with six of the ten symptoms (i.e.,

pain, fatigue, sleep disturbance, cognitive concerns, anxiety, and depressive symptoms) as well as value obstruction. Conversely, greater psychological inflexibility was related to less value progress and engagement in roles and activities.

Primary analyses

A hierarchical agglomerative cluster analysis was conducted to derive participant clusters based on the severity of the ten symptoms. A 3-cluster solution was found. Cluster 1 was labeled “Low Symptoms,” as it comprised 47 people with low symptom levels across domains. Cluster 2 was labeled “Low-Moderate Symptoms” and comprised 14 people with low to moderate symptom levels across domains. Cluster 3 was labeled “Moderate-High Symptoms,” as 19 people reported moderate to high symptom levels across domains. No significant differences were found among the clusters on demographic variables (i.e., age, income, education, employment status, and marital status) and medical factors (i.e., surgery, radiation, chemotherapy, hormonal therapy, and time since diagnosis).

One-way ANOVAs revealed significant differences between clusters on ratings of the ten symptoms (see Table 3). Tukey’s post hoc comparisons showed that Cluster 1 frequently had lower symptom levels than the other clusters, and Cluster 2 had lower symptom levels than Cluster 3 for hot flashes and fatigue.

One-way ANOVAs also revealed significant differences between clusters on activity engagement, psychological inflexibility, and value obstruction (see Table 3). Tukey’s comparisons showed that Cluster 1 had greater activity engagement than the other clusters, which did not significantly differ from each other. Tukey’s comparisons also showed that Cluster 1 had lower levels of psychological inflexibility and value obstruction than Cluster 3. The three clusters did not differ from each other with respect to value progress.

Conclusions

This study is the first to identify subgroups of patients with MBC based on ratings of common symptoms and their associations with key ACT constructs (i.e., activity engagement, psychological inflexibility, value obstruction, and value progress). Results suggested that there were three patient subgroups: those with low symptoms, low-moderate symptoms, and moderate-high symptoms. Prior research with other cancer populations has also found heterogeneity with respect to patients’ symptom experience [40]. In this study, compared to patients with low symptoms, the other patient subgroups reported less activity engagement. Furthermore, relative to patients with low symptoms, the subgroup with moderate to high symptom levels reported greater psychological inflexibility (i.e., avoidance of unwanted internal experiences) and greater difficulty living a life consistent with their values. These results are largely consistent with ACT theory [17] and suggest that MBC patients with greater symptom burden may be more likely to avoid unwanted thoughts, emotions, and sensations and withdraw from valued activities and relationships. These patients may be targeted in future research examining ACT interventions for symptom interference.

Two prior studies of patients with various cancer types and stages have linked greater avoidance of unwanted experiences or psychological inflexibility to worse physical and emotional well-being and greater psychological distress [21, 22]. The present findings extend this work by linking this avoidance to a variety of physical and psychological symptoms in a sample of advanced cancer patients. One explanation for these findings is that patients may cope with their high symptom burden by attempting to avoid aversive thoughts, feelings, and sensations. Alternatively, attempts to avoid symptoms may exacerbate them, as patients may not seek necessary support or may use ineffective methods of symptom control (e.g., excessive resting instead of engaging in meaningful activities). A third account of the findings is that a common unmeasured factor (e.g., emotional reactivity) may drive symptom perceptions and psychological inflexibility.

Another key finding of this study was that greater psychological inflexibility and higher symptom levels were related to reduced activity engagement and greater value obstruction. Similarly, a prior study of cancer patients found that greater psychological inflexibility was associated with less success in value-based living in certain domains (e.g., family, leisure) [21]. Consistent with these findings, ACT theorists have proposed that psychological suffering results from attempts to avoid aversive experiences, such as symptoms, which often lead to disengagement from valued activities [17].

Whereas value obstruction was associated with patient subgroups based on symptoms, progress in valued-based living was not. However, greater progress in value-based living was associated with lower levels of certain symptoms (e.g., fatigue, sleep disturbance, anxiety, and depressive symptoms), most of which were symptoms that characterize many psychological disorders. These findings underscore the importance of separately examining progress and obstructions to value-based living in MBC patients when predicting symptom outcomes. Future longitudinal research may examine whether value obstruction is more predictive of poor symptom outcomes than value progress.

The present findings have important implications for future research and clinical practice with MBC patients. First, our findings in combination with prior descriptive research on ACT constructs in cancer patients [21, 22] provide an empirical basis for examining interventions such as ACT that aim to improve acceptance of internal experiences and engagement in activities consistent with personal values. Results of one pilot trial suggest that ACT produces large improvement in mood and quality of life in advanced ovarian cancer patients [27]; thus ACT warrants investigation as an approach to reducing symptom interference in MBC patients. Additionally, our results point to the need to tailor interventions to patient characteristics. For example, if replicated, findings would suggest that patients in the “Low-Moderate Symptoms” and “Moderate-High Symptoms” subgroups may benefit from intervention to reduce the impact of their symptoms on activities. Further research is needed to determine whether symptomatic patients with high levels of psychological inflexibility benefit from acceptance-based approaches (e.g., ACT) to symptom interference in conjunction with standard symptom management.

Limitations of this study and directions for future research should be noted. The sample primarily consisted of highly educated, Caucasian patients. Future research should examine

the degree to which findings generalize to MBC patients with diverse socioeconomic and ethnic backgrounds. In addition, the cross-sectional design precluded an assessment of temporal relationships among variables. Longitudinal research is needed to determine whether ACT variables such as psychological flexibility predict symptom outcomes. Such research may include other variables central to ACT, such as cognitive defusion, mindfulness, value-based living in specific domains, and acceptance, to more fully examine the ACT model of symptom interference in MBC patients. Finally, certain symptoms (e.g., nausea) may have been unrelated to some ACT constructs in this study due to range restriction; larger samples are needed to ensure symptom heterogeneity for predicting outcomes.

Despite commonly used pharmacologic approaches to symptom management, MBC patients have high symptom burden that is a major source of suffering, impairment, and disability [2–4, 6]. Standard non-pharmacologic approaches such as cognitive-behavioral therapy show limited evidence for reducing the symptom-related suffering of MBC patients [16]. ACT differs from traditional cognitive-behavioral approaches by emphasizing mindfulness, acceptance, and actions based on personal values. The current findings in combination with prior research [21, 22, 26] support investigating ACT as an intervention to reduce symptom interference and promote value-based living in this population.

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Table 1

Sample characteristics ($N = 80$)

Characteristic	
Age (years)	
Mean (SD)	55.50 (11.26)
Range	32–80
Years of education	
Mean (SD)	15.03 (2.42)
Range	11–20
Years since the stage IV breast cancer diagnosis	
Mean (SD)	3.93 (3.64)
Range	0.21–19.46
Ethnicity, no. (%)	
Non-Hispanic White	73 (91.3)
Other ethnicity[a]	7 (8.8)
Married or partnered, no. (%)	53 (66.3)
Employed, no. (%)	24 (30.0)
Household income, no. (%)	
$0 – $30,999	17 (21.8)
$31,000 – $50,999	18 (23.1)
$51,000 – $99,999	26 (33.3)
$100,000 +	17 (21.8)
Cancer treatment history, no. (%)	
Chemotherapy	69 (86.3)
Radiation	52 (65.0)
Hormonal therapy	68 (85.0)
Mastectomy	53 (66.3)
Lumpectomy	17 (21.3)

SD = standard deviation.

[a]African American/Black, Hispanic, and other.

Table 2

Descriptive statistics and intercorrelations for main study variables

		1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	Nausea														
2	Neuropathy	0.33**													
3	Swelling of arms or legs	0.21	0.30**												
4	Hot flashes	0.14	−0.05	−0.21											
5	Pain	0.33**	0.38**	0.29**	0.19										
6	Fatigue	0.33**	0.29**	0.11	0.26*	0.52**									
7	Sleep disturbance	0.28*	0.15	0.12	0.21	0.34**	0.50**								
8	Cognitive concerns	0.21	0.26*	0.07	0.13	0.20	0.64**	0.51**							
9	Anxiety	0.17	0.19	0.09	0.23*	0.27*	0.52**	0.46**	0.44**						
10	Depressive symptoms	0.33**	0.14	0.20	0.08	0.34**	0.50**	0.44**	0.39**	0.71**					
11	Ability to participate in social roles and activities	−0.21	−0.20	−0.33**	−0.14	−0.52**	−0.68**	−0.38**	−0.38**	−0.38**	−0.43**				
12	Psychological inflexibility	0.18	0.17	0.10	0.18	0.24*	0.56**	0.50**	0.53**	0.75**	0.68**	−0.36**			
13	Value progress	−0.27*	−0.02	0.06	−0.12	−0.11	−0.33**	−0.31**	−0.22	−0.36**	−0.41**	0.37**	−0.45**		
14	Value obstruction	0.20	0.25*	0.14	0.13	0.28*	0.54**	0.42**	0.44**	0.61**	0.56**	−0.38**	0.77**	−0.38**	
	Mean	0.63	1.13	0.46	1.64	6.60	11.39	11.10	11.43	7.33	6.65	19.60	13.66	23.14	6.15
	Standard deviation	0.91	1.19	0.87	1.92	2.65	4.31	3.90	5.11	3.14	3.20	6.20	7.28	5.79	6.19
	Cronbach's α	0.95	0.89	0.91	0.75	0.83	0.92	0.84	0.95	0.86	0.90	0.95	0.91	0.86	0.86

* $p < 0.05$.

** $p < 0.01$.

Table 3

Symptoms and ACT variables by participant clusters

	Low symptoms (L) (*n* = 47)		Low-Moderate symptoms (L/M) (*n* = 14)		Moderate-High symptoms (M/H) (*n* = 19)		*F*	*p*
	Mean	SD	Mean	SD	Mean	SD	Tukey's post-hoc comparisons[a]	
Symptom								
Nausea	0.18	0.47	1.05	0.88	1.44	1.11	22.21	< .001
							L < L/M	.001
							L < M/H	< .001
Neuropathy	0.55	0.82	2.07	0.95	1.88	1.29	20.76	< .001
							L < L/M and M/H	< .001
Swelling of arms or legs	0.10	0.36	2.04	0.75	0.18	0.48	95.24	< .001
							L and M/H < L/M	< .001
Hot flashes	1.35	1.72	0.32	0.87	3.32	1.88	14.97	< .001
							L < M/H	< .001
							L/M < M/H	< .001
Pain	5.21	2.06	8.07	1.59	8.95	2.34	26.48	< .001
							L < L/M and M/H	< .001
Fatigue	9.66	3.94	11.86	2.74	15.32	3.51	16.28	< .001
							L < M/H	< .001
							L/M < M/H	.024
Sleep disturbance	9.98	3.34	11.29	3.31	13.74	4.45	7.30	.001
							L < M/H	.001
Cognitive concerns	10.13	5.03	12.07	4.71	14.16	4.62	4.75	.011
							L < M/H	.009
Anxiety	6.30	2.49	8.14	3.53	9.26	3.35	7.73	.001

	Low symptoms (L) (*n* = 47)		Low-Moderate symptoms (L/M) (*n* = 14)		Moderate-High symptoms (M/H) (*n* = 19)		*F*	*p*
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Tukey's post-hoc comparisons[a]**	
							L < M/H	.001
Depressive symptoms	5.43	1.81	8.43	4.07	8.37	3.88	10.32	< .001
							L < L/M	.003
							L < M/H	.001
ACT variable								
Ability to participate in social roles and activities	21.79	6.31	16.36	3.67	16.58	5.19	8.42	< .001
							L > L/M	.007
							L > M/H	.003
Psychological inflexibility	11.21	5.30	15.93	6.55	18.05	9.50	7.99	.001
							L < M/H	.001
Value progress	24.00	5.47	22.93	4.50	21.21	7.08	1.59	.210
Value obstruction	4.28	4.56	7.86	5.33	9.53	8.42	6.25	.003
							L < M/H	.004

[a]Only significant Tukey comparisons are reported. SD = standard deviation. ACT = Acceptance and Commitment Therapy.

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